

# PATENT COOPERATION TREATY

## PCT

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### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference  P025931WO	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No.  PCT/GB01/04789	International filing date (day/month/year)  29/10/2001	Priority date (day/month/year)  27/10/2000	
International Patent Classification (IPC) or national classification and IPC  C07K14/195			
Applicant  CHIRON S.P.A. et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I    Basis of the report
- II    Priority
- III    Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV    Lack of unity of invention
- V    Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI    Certain documents cited
- VII    Certain defects in the international application
- VIII    Certain observations on the international application

Date of submission of the demand  23/05/2002	Date of completion of this report  17.02.2003
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Marinoni, J-C  Telephone No. +49 89 2399 8563



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB01/04789

## I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

### Description, pages:

1-3023                  as originally filed

### Claims, No.:

1-28                  as originally filed

### Claims, pages:

3024-3030,3032-3037,                  as originally filed  
3039-3046,  
3048-3057

3031,3047                  as received on                  18/12/2002 with letter of                  18/12/2002

3038                  as received on                  24/01/2003 with letter of                  24/01/2003

### Drawings, sheets:

1/95-95/95                  as originally filed

### Sequence listing part of the description, pages:

1-1372, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

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- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description,        pages:
- the claims,           Nos.:
- the drawings,        sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application.
- claims Nos. 19-22 completely; 17, 26 partially.

because:

- the said international application, or the said claims Nos. 17 partially relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 19-22 completely; 26 partially are so unclear that no meaningful opinion could be formed (*specify*):  
**see separate sheet**
- the claims, or said claims Nos. 19-22 completely; 26 partially are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. 22 completely; 26 partially.

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2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- the written form has not been furnished or does not comply with the standard.
- the computer readable form has not been furnished or does not comply with the standard.

## IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- restricted the claims.
- paid additional fees.
- paid additional fees under protest.
- neither restricted nor paid additional fees.

2.  This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- complied with.
- not complied with for the following reasons:  
**see separate sheet**

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- all parts.
- the parts relating to claims Nos. 1-7,9-18,23-28.

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)	Yes:	Claims 1-7,9,10,18,27
	No:	Claims 11-17,23-26,28
Inventive step (IS)	Yes:	Claims 1,3,7,18
	No:	Claims 2, 4-6,9-17,23-28
Industrial applicability (IA)	Yes:	Claims 1-16,18,23-28
	No:	Claims 17

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2. Citations and explanations  
see separate sheet

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**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. **Claim 22** is directed to a computer-readable medium which amounts to the mere presentation of information. Examination of such subject-matter is not required (see Article 34(4)(a)(i) and Rule 67.1(v) PCT). Moreover the subject-matter of said claim was not searched according to Rule 39.1(v) PCT. Therefore, examination of said subject-matter is not carried out in the present report.
2. **Claim 26** is directed to subject-matter which finds no support of technical nature (Article 6 PCT) and is not sufficiently disclosed (Article 5 PCT) over the entire range claimed. Search was restricted to antibodies to the claimed proteins. Examination is carried out only for said subject-matter.
3. **Claim 17** partially relates to treatment of the animal/human body by therapy. Examination is not required for said subject-matter (see Article 34(4)(a)(i) and Rule 67.1(iv) PCT). Examination is only carried out regarding the alleged effect of the compounds referred to in the claim.
4. It is considered that the subject-matter covered by **claims 19-21** is so vaguely defined, that virtually any pair of primer falls into the scope of the claim, contrary to Article 6 PCT, that no examination can be carried out regarding the subject-matter of said claims.

**Re Item IV**

**Lack of unity of invention**

1. The ISA raised an objection for lack of unity of the invention under Rule 13 PCT and subsequently identified more than 6500 groups of inventions. Following the payment of 3 additional search fees, the search has been restricted to the inventions of examples 1245 (SEQ ID No. 3849, 3850, 8769, 8770), 679 (SEQ ID No. 2091, 2092, 2093, 2094, 8637, 8638), 498 (SEQ ID No. 1593, 1594, 8583, 8584) and 67 (SEQ ID No. 215, 216, 217, 128).
2. The separate groups of invention are therefore:
  - (i) the nucleic and amino acid sequences of example 1245 (SEQ ID No. 3849,

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3850, 8769, 8770), antibodies, compositions, processes and methods related thereto.

- (ii) the nucleic and amino acid sequences of example 679 (SEQ ID No. 2091, 2092, 2093, 2094, 8637, 8638), antibodies, compositions, processes and methods related thereto.
- (iii) the nucleic and amino acid sequences of example 498 (SEQ ID No. 1593, 1594, 8583, 8584), antibodies, compositions, processes and methods related thereto.
- (iv) the nucleic and amino acid sequences of example 67 (SEQ ID No. 215, 216, 217, 128), antibodies, compositions, processes and methods related thereto.

3. They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

The present application relates to proteins from group B *Streptococcus* (*S. agalactiae*) and from group A *Streptococcus* (*S. pyogenes*) that are allegedly useful antigens for vaccines, immunogenic compositions and/or diagnostics, and also targets for antibiotics.

Proteins from group A and group B *Streptococci*, in particular *S. agalactiae* and *S. pyogenes* are known from the art. Therefore, two main groups of inventions are present in the application.

Additionally, proteins of *S. agalactiae* and *S. pyogenes* useful as antigens for vaccines, immunogenic compositions and/or diagnostics are known from the art (see *inter alia* D4 for *S. agalactiae* or D5 for *S. pyogenes*).

4. The nucleic acids/proteins can somehow be grouped according to their sequence for the reason that homologues of a given nucleic acids/proteins found in *S. pyogenes* were found in *S. agalactiae* (see the examples). However, it is still considered that these constitute separate invention since they do not share a common inventive feature, *i.e.* a special technical feature in the sense of Article 13 PCT. However, due to the sequence similarities, examination can be performed for each of the identified groups of inventions provided that additional fees are timely paid.

5. The Applicant chose not to pay additional fees and restricted the subject-matter to be examined to group of inventions (iii), *i.e.* **claims 1-7, 9-18, 23-28 all partially**.

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**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Cited documents**

**D1:** DATABASE GENESEQ, 9 November 1998, BLACK M T ET AL.:

'Streptococcus pneumoniae polypeptide coding region' Database accession no. AAV42990 & WO 98 23631, 4 June 1998

**D2:** DATABASE EMBL, 6 May 1999, MEEHAN MC & OWEN P: 'Sequence 1 from Patent WO9801561' Database accession no. A68631 & WO 98 01561, 15 January 1998

**D3:** WO9916882

**D4:** MICHEL J L ET AL: 'Cloned alpha and beta C-protein antigens of group B Streptococci elicit protective immunity' INFECTION AND IMMUNITY, AMERICAN SOCIETY FOR MICROBIOLOGY, vol. 59, no. 6, June 1991, pages 2023-2028

**D5:** STALHAMMAR-CARLEMALM M ET AL: 'THE R28 PROTEIN OF STREPTOCOCCUS PYOGENES IS RELATED TO SEVERAL GROUP B STREPTOCOCCAL SURFACE PROTEINS, CONFER PROTECTIVE IMMUNITY AND PROMOTES BINDING TO HUMAN EPITHELIAL CELLS' MOLECULAR MICROBIOLOGY, vol. 33, no. 1, July 1999, pages 208-219

- 2.** None of the available documents discloses a protein having the sequences of SEQ ID No. 1594 or 8584, or the nucleic acids encoding them or proteins having at least 12 identical consecutive amino acids the sequences of SEQ ID No. 1594 or 8584, or nucleic acids having more than 12 consecutive identical nucleotides. Therefore, the subject-matter of **claims 1-7, 9, 10, 18, 27** meets the requirements of Article 33(2) PCT concerning novelty.
- 3.** **D1, D2 and D3** disclose nucleic acids encoding *S. pneumoniae*, *S. equi*, *S. agalactiae* proteins respectively and having 54%, 53% and 63% identity respectively with the sequence of SEQ ID No. 1593, and are hybridizable thereto. The subject-matter of **claims 11 and 12** is therefore not novel. Consequently, the subject-matter of **claims 13-17 and 23-26 and 28** does not meet the requirements of Article 33(2) PCT concerning novelty.

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4. The specific sequences of SEQ ID No. 1594 and 8584 appear to involve an inventive step since it is demonstrated in the present application that they induce protective immunity against *S. agalactiae* on the one hand and *S. pyogenes* on the other hand. Therefore, the subject-matter of **claims 1, 7 and 18** appears to meet the requirements of Article 33(3) PCT.
5. It is doubtful that the proteins defined by way of a percentage of identity all solve the technical problem underlying the application, *i.e.* confer protective immunity against *S. agalactiae* or *S. pyogenes*. It is obvious that the specific protein of the invention are inventive since they inherently solve this technical problem, and therefore meet the requirements of Article 33(3) PCT concerning inventive step. Fragments of these proteins defined by the fact that they contain more than 12 consecutive amino acids and that they confer protective immunity (**claim 3**) meet the requirements of Article 33(3) PCT too for the same reason.  
However; the protein of **claim 2** is defined only by the fact that it has at least 60% identity to the protein of SEQ ID No. 1594/8584 without any functional limitation. The scope of the claim therefore embraces proteins which do not necessarily solve the technical problem underlying the present invention, but merely solve the technical problem of providing new amino acid sequences. The provision of new amino acid sequence which do not solve a specifically identified technical problem is not inventive. Consequently, the antibodies of **claim 4-5** and the nucleic acid of **claim 6** do not involve an inventive step, when referring back to claim 2. The subject-matter of **claim 2, 4-5 and 6** therefore does not meet the requirements of Article 33(3) PCT concerning inventive step.  
The same objection applies *mutatis mutandis* to the subject-matter of **claim 9** which is directed to nucleic acids fragments comprising at least 12 nucleotide of the SEQ ID No. 1583/8583.  
As a consequence, the subject-matter of **claims 10-17 and 23-28** is not inventive when referring back to any of **claims 2, 4-6 or 9**.  
Therefore, they cannot be considered as involving an inventive step.  
Consequently, the subject-matter of **claims 2, 4-6, 9-17, 23-28** does not meet the requirements of Article 33(3) PCT concerning inventive step.
6. It should be made clear in the claims that the protective immunity conferred by the proteins of the invention is effective against *S. agalactiae* or *S. pyogenes*.

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10900, 10902, 10904, 10906, 10908, 10910, 10912, 10914, 10916, 10918, 10920, 10922, 10924, 10926, 10928,  
10930, 10932, 10934, 10936, 10938, 10940, 10942, 10944, 10946, 10948, 10950, 10952, 10954, 10956, 10958,  
10960, 10962, 10964 and 10966.

2. A protein having 60% or greater sequence identity to a protein according to claim 1.

5       3. A protein comprising a fragment of 12 or more consecutive amino acids from an amino acid sequence selected  
from the group consisting of SEQ IDs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44,  
46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104,  
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10     198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242,  
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30     1092, 1094, 1096, 1098, 1100, 1102, 1104, 1106, 1108, 1110, 1112, 1114, 1116, 1118, 1120, 1122, 1124, 1126,  
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1560, 1562, 1564, 1566, 1568, 1570, 1572, 1574, 1576, 1578, 1580, 1582, 1584, 1586, 1588, 1590,

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12009, 12010, 12011, 12012, 12013, 12014, 12015, 12016, 12017, 12018, 12019, 12020, 12021, 12022, 12023  
and 12024.

9. A nucleic acid molecule comprising a fragment of 12 or more consecutive nucleotides from a nucleotide sequence selected from the group consisting of SEQ IDs 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43,  
5 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105,  
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20 779, 781, 783, 785, 787, 789, 791, 793, 795, 797, 799, 801, 803, 805, 807, 809, 811, 813, 815, 817, 819, 821, 823, 825,  
827, 829, 831, 833, 835, 837, 839, 841, 843, 845, 847, 849, 851, 853, 855, 857, 859, 861, 863, 865, 867, 869, 871, 873,  
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4. An antibody which binds to a protein according to any one of claims 1 to 3.

5. The antibody of claim 4, wherein said antibody is a monoclonal antibody, a chimeric antibody, a humanised antibody, or a fully human antibody.

10 6. A nucleic acid molecule which encodes a protein according to any one of claims 1 to 3.

7. A nucleic acid molecule according to claim 6, comprising a nucleotide sequence selected from the group consisting of SEQ IDs 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 15 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407, 409, 411, 413, 20 415, 417, 419, 421, 423, 425, 427, 429, 431, 433, 435, 437, 439, 441, 443, 445, 447, 449, 451, 453, 455, 457, 459, 461, 463, 465, 467, 469, 471, 473, 475, 477, 479, 481, 483, 485, 487, 489, 491, 493, 495, 497, 499, 501, 503, 505, 507, 509, 511, 513, 515, 517, 519, 521, 523, 525, 527, 529, 531, 533, 535, 537, 539, 541, 543, 545, 547, 549, 551, 553, 555, 557, 559, 561, 563, 565, 567, 569, 571, 573, 575, 577, 579, 581, 583, 585, 587, 589, 591, 593, 595, 597, 599, 601, 603, 605, 607, 609, 611, 613, 615, 617, 619, 621, 623, 625, 627, 629, 631, 633, 635, 637, 639, 641, 643, 645, 647, 649, 651, 653, 655, 657, 659, 661, 663, 25 665, 667, 669, 671, 673, 675, 677, 679, 681, 683, 685, 687, 689, 691, 693, 695, 697, 699, 701, 703, 705, 707, 709, 711, 713, 715, 717, 719, 721, 723, 725, 727, 729, 731, 733, 735, 737, 739, 741, 743, 745, 747, 749, 751, 753, 755, 757, 759, 761, 763, 765, 767, 769, 771, 773, 775, 777, 779, 781, 783, 785, 787, 789, 791, 793, 795, 797, 799, 801, 803, 805, 807, 809, 811, 813, 815, 817, 819, 821, 823, 825, 827, 829, 831, 833, 835, 837, 839, 841, 843, 845, 847, 849, 851, 853, 855, 857, 859, 861, 863, 865, 867, 869, 871, 873, 875, 877, 879, 881, 883, 885, 887, 889, 891, 893, 895, 897, 899, 901, 903, 905, 907, 909, 911, 913, 30 915, 917, 919, 921, 923, 925, 927, 929, 931, 933, 935, 937, 939, 941, 943, 945, 947, 949, 951, 953, 955, 957, 959, 961, 963, 965, 967, 969, 971, 973, 975, 977, 979, 981, 983, 985, 987, 989, 991, 993, 995, 997, 999, 1001, 1003, 1005, 1007, 1009, 1011, 1013, 1015, 1017, 1019, 1021, 1023, 1025, 1027, 1029, 1031, 1033, 1035, 1037, 1039, 1041, 1043, 1045, 1047, 1049, 1051, 1053, 1055, 1057, 1059, 1061, 1063, 1065, 1067, 1069, 1071, 1073, 1075, 1077, 1079, 1081, 1083, 1085, 1087, 1089, 1091, 1093, 1095, 1097, 1099, 1101, 1103, 1105, 1107, 1109, 1111, 1113, 1115, 1117, 1119, 1121, 1123, 1125, 1127, 1129, 1131, 35 1133, 1135, 1137, 1139, 1141, 1143, 1145, 1147, 1149, 1151, 1153, 1155, 1157, 1159, 1161, 1163, 1165, 1167, 1169, 1171, 1173, 1175, 1177, 1179, 1181, 1183, 1185, 1187, 1189, 1191, 1193, 1195, 1197, 1199, 1201, 1203, 1205, 1207, 1209, 1211, 1213, 1215, 1217, 1219, 1221, 1223, 1225, 1227, 1229, 1231, 1233, 1235, 1237, 1239, 1241, 1243, 1245, 1247, 1249, 1251, 1253, 1255, 1257, 1259, 1261, 1263, 1265, 1267, 1269, 1271, 1273, 1275, 1277, 1279, 1281, 1283, 1285, 1287, 1289, 1291, 40 1293, 1295, 1297, 1299, 1301, 1303, 1305, 1307, 1309, 1311, 1313, 1315, 1317, 1319, 1321, 1323, 1325, 1327, 1329,